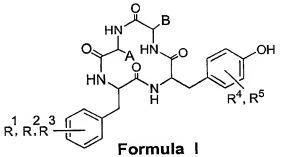
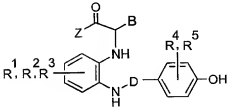
ABSTRACT

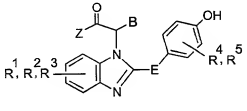
The invention relates to new basic amino acid derivatives of general formulae I, II and III, and the preparation and use thereof in treatment of pain. The compounds have histogranin-like antinociceptive, morphine potentiating and COX-2 induction modulating activities.



Formula I



Formula II



Formula III

wherein:

A is -hydrogen, -(C_1-C_8)alkyl or -(C_1-C_8)alkyl substituted by hydroxy;

B is -(C_1-C_6)alkylguanidino, -(C_1-C_6)alkyl(4-imidazolyl), -(C_1-C_6)alkylamino, p-aminophenylalkyl(C_1-C_6)-, p-guanidinophenylalkyl(C_1-C_6)- or 4-pyridinylalkyl(C_1-C_6)-;

D is -(CO)-, -(CO)-(C_1-C_6)alkylene or -(C_1-C_6)alkylene;

E is a single bond or -(C_1-C_6)alkylene;

Z is $-NH_2$, -NH-(C_1-C_6)alkylcarboxamide, -NH-(C_1-C_6)alkyl, -NH-(N-benzyl), -NH-cyclo(C_5-C_7)alkyl, -NH-2-(1-piperidyl)ethyl, -NH-2-(1-pyrrolidyl)ethyl, -NH-2-(1-pyridyl)ethyl, -NH-2-(morpholino)ethyl, -morpholino, -piperidyl, -OH, -(C_1-C_6)alkoxy, -O-benzyl or -O-halobenzyl;

R^1, R^2 and R^3 are, independent of one another, -hydrogen, -arylcarbonylamino, -(C_1-C_6)alkoylamino, -(C_1-C_6)alkylamino, -(C_1-C_6)alkyloxy, -(C_1-C_6)alkylaminocarbonyl, -carboxy, -OH, -benzoyl, -p-halogenobenzoyl, -methyl, -S-(2,4-dinitrophenyl), -S-(3-nitro-2-pyridinesulfenyl), -sulfonyl, -trifluoromethyl, -(C_1-C_6)alkylaminocarbonylamino, -halo or -amino;

R^4 and R^5 are, independent of one another, -hydrogen, -(C_1-C_6)alkyl, -methyloxy, -nitro, -amino, -arylcarbonylamino, -(C_1-C_6)alkoylamino, -(C_1-C_6)alkylamino, -halo or -OH.